REMARKS

I. Status of the Claims

Claims 18, 19, 22, 28, 29, 31, 32, 38, 39, 42, 53-56 and 65-67 are pending in the application. The claims stand rejected under 35 U.S.C. §112, 35 U.S.C. §102 and 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

Applicants have now twice requested an interview with the examiner. And twice, the examiner has not called the undersigned upon receipt of applicants' submissions. Applicants once again respectfully request, that upon consideration of this response, the examiner contact the undersigned to discuss any unresolved issues.

II. Rejections Under 35 U.S.C. §112, First Paragraph

Claims 22 and 42 stand rejected under the first paragraph of §112 as lacking an enabling disclosure. Applicants traverse. The examiner argues that claim 42 and claim 22, from which claim 42 depends, permit the possibility of a single CDR or portion thereof. This is incorrect. Both claims 22 and 42 depend from claim 18, and claim 18 requires VH and VL regions, and as such, comprise all 6 CDRs. Thus, claims 22 and 42 ***cannot***, by definition, have less than all 6 CDRs. Reconsideration and withdrawal of the rejection is therefore requested.

Claims 18 and 28 are said to lack written description, and contain new matter, in light of the language "native human 17-1A antigen." Applicants traverse, but in the interest of advancing the prosecution, the claims have been amended to recite "human 17-1A antigen as expressed on the surface of cells," thereby obviating the rejection. Support for the amendment

may be found at pages 8 and 15 of the specification. Reconsideration and withdrawal of the rejection is therefore requested.

III. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 18 and 28 stand rejected under the second paragraph of §112 for the continued use of "the receptor." Appropriate amendments have been made.

Claims 18 and 28 stand rejected under the second paragraph of §112 for use of the term "native human 17-1A antigen." The claims have been amended to recite "human 17-1A antigen as expressed on the surface of cells," thereby obviating the rejection. Support for the amendment may be found at pages 8 and 15 of the specification.

Reconsideration and withdrawal of each of the foregoing amendments is therefore respectfully requested.

IV. Rejection Under 35 U.S.C. §102

Claims 18-21 and 34-37 remain rejected over Hoess *et al.* ("Hoess"). As discussed by the examiner, Hoess teaches antibodies which bind human 17-1A antigen. However, the examiner is wrong in stating that Hoess describes antibodies that bind to ***native*** human 17-1A, and on this basis, applicant traverses. A careful review of the reference will reveal that Hoess tests antibodies produced from a combinatorial library, having two different specificities – for 17-1A and LeY. Although antibodies that bound 17-1A were identified, these antibodies bound only to ***immobilized antigen*** and did not recognize cancer cells. To the contrary, the anti-LeY antibodies ***did*** reocognize cancer cells. This distinction indicates that the antibodies to 17-1A did ***not*** recognize native antigen, and thus, could not anticipate the presently claimed invention. In further support of this position, applicant points to de Kruif *et al.* (1995), at page 101, which

states "None of the MoPhabs against ICAM-1 or δEGP-2 displayed binding to cells expressing these molecules ...." Thus, this reference teaches that these researchers failed to generate and isolate an anti-17-1A (there called EGP-2) antibody that recognized the native antigen.

The examiner denies that the foregoing is true. Attached to this response is the declaration of the inventor, Dr. Kufer, who was a coauthor on the Hoess *et al.* paper. Therein, Dr. Kufer states that the human 17-1A-specific antibody fragments described in the reference were only reactive with recombinant 17-1A (EpCAM), and failed to bind human 17-1A ***as expressed on the surface of cells (i.e., native 17-1A)***. Morever, the significance of the de Kruif *et al.* (1995) paper is to note both (a) the well-known phenomenon that antibodies or fragments thereof isolated from combinatorial antibody libraries often bind to recombinant antigen, but do not necessarily bind to native antigens (*i.e.*, antigens expressed on the surface of cells), and (b) that the antibodies produced by those authors similarly failed to react with native 17-1A antigen.

Moreover, the examiner is directed to lines 1 to 10 from bottom of the Hoess *et al.* abstract. The relevant passage reads as follows: "To create multivalent antibodies displaying high affinities for cell surface antigens, scFv's can be fused .... The scFv4 recognizes specifically cancer cells overexpressing LeY compared to ...." No equivalent antibody construct specifically recognizing cancer cells expressing 17-1A antigen could be obtained, however. Consequently, the only proper conclusion is that the cited abstract does not report on such antibodies. As such, reconsideration and withdrawal of the rejection is respectfully requested.

V. Rejections Under 35 U.S.C. §103

Claims 18-21, 34-41, 43-46, 48-51, 65 and 67 remain rejected as obvious over the '584 patent in view of Gottlinger. Both references are cited as above. Applicants once again traverse.

As argued previously, the rejection fails due to the difficulty, and hence lack of predictability, of creating human anti-17-1A antibodies. This was based upon the ubiquity of the antigen and self tolerance. In response, the examiner now argues that the methods of the '584 patent do not rely on creating a human antibody, but rather, a mouse antibody that reacts with a human antigen. Applicants traverse.

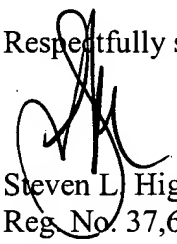
Human antibodies recognizing the human 17-1A antigen, as expressed on the surface of cells, could not, at the time the present application was filed, be obtained from the human-Ig transgenic mice used in the procedure set out in the '584 patent. The reason is that the transgenic mice of the '584 patent carry a human Ig-repertoire – the same repertoire that is found in humans – and this is evolutionarily biased against conserved self antigens such as 17-1A. Thus, the same under-representation of undesired self specificities like 17-1A will appear in the transgenic mice of the '584 patent, just as in a real human Ig-repertoire that is evolutionarily biased to avoid such specificities. Accordingly, even today, there is still no report in the literature on human antibodies against human 17-1A from human Ig-transgenic mice, although human antibodies against many other less ubiquitous human antigens have been successfully generated using the '584 patent's methods. See attached declaration from Dr. Kufer (paras. 4-6).

Thus, in light of the foregoing consideration, reconsideration and withdrawal of the rejection is again respectfully requested.

VI. Conclusion

All claims are believed to be in condition for allowance, and an early notification to that effect is earnestly solicited. Should Examiner Helms have any questions regarding this response, a telephone call to the undersigned is invited. Please date stamp and return the enclosed postcard as evidence of receipt.

Respectfully submitted,



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